

REMARKS/ARGUMENTS

I. Status of the Claims

Claims 66-89, 109-111, 113, and 118-125 are currently pending. Claims 69-89 have been withdrawn from consideration as being directed to a non-elected invention. Claims 66-68, 109-111, 113, and 118-125 are under consideration. Claims 118-125 are new. Claims 112 and 114-117 are canceled. Claims 66-67, 109-110, and 113 are currently amended.

II. The Invention

Interactions between recognition moieties, which are components of an organic layer, and analytes can be amplified and transduced into optical signals through the use of a mesogenic layer. This invention provides a device for detecting these analyte-recognition moiety interactions.

As presently claimed, the device comprises a substrate onto which an organic layer is attached and a mesogenic layer which is anchored by the organic layer. An interaction between a recognition moiety and an analyte introduces a change in the orientation of the organic layer, which is subsequently transduced to the mesogens of the mesogenic layer. Interaction-induced changes in the intensity of light transmitted through the mesogenic layer are then detected.

III. Support for the Amendments

Support for the amendments to the claims can be found throughout the specification and the claims as originally drafted.

Claims 66 and 109 are amended to recite a first organic layer comprising a first recognition moiety which is bound to the first organic layer. Support for this amendment is found in Examples 1-5.

Claim 67 is amended to recite avidin as an analyte. Support for this amendment is found in Example 1.

Claims 66 and 109 are also amended to recite "first" surfaces of a first substrate and "second" surfaces of a second substrate. These amendments are correcting minor typographical errors.

Claim 109 is selected from an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, and a cyclodextrin. Support for this amendment is found in the specification on page 37, lines 15-29; page 38, line 1 to page 40 line 12 page 27; and page 42 line 26 to page 43, line 14.

Claim 110 is amended to provide proper support for "interior portion", which lacked antecedent basis in the original version. This amendment is correcting a minor typographical error.

Claim 113 is amended to change the claim dependency from cancelled claim 112 to claim 109. In addition, claim 113 is amended to remove 'proteins' as a potential biomolecule. These amendments are correcting minor typographical errors.

Claim 66 is also amended to replace the word "presence", which had no antecedent basis in the claim, with the word "interaction", which has an antecedent basis in the claim. This amendment corrects a minor typographical error.

IV. The New Claims

Claims 118-125 are new. Claims 118-120 generally mirror the claim limitations of claims 66-68. The major difference is that claims 118-120 contain a second recognition moiety on the second organic layer. This second recognition moiety is selected from amines, carboxylic acids, biomolecules, drug moieties, chelating agents, crown ethers, and cyclodextrins. Support for these new claims is provided in Examples 1, 4, and 5.

Claims 121-124 specify that the organic layer comprises a self-assembled organosulfur or organosilane monolayer (SAM) bound to a surface. Bound to the self-assembled monolayer is a recognition moiety. Support for these new claims is provided in Examples 1-5.

Claim 125 specifies that the first recognition moiety is selected from an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, and a

cyclodextrin. Support for this amendment is found in the specification on page 37, lines 15-29; page 38, line 1 to page 40 line 12 page 27; and page 42 line 26 to page 43, line 14.

V. Responses to the Claim Rejections

Under 35 U.S.C. § 102

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record. Therefore, Applicants respectfully traverse the following rejections.

Under 35 U.S.C. § 102(a)

Claims 66-68, 109-110 and 114-115 are rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Gupta *et al.*, *Science*, **279**:2077-2080 ("Gupta"). Gupta is cited for teaching a liquid cell assembly comprising two separate gold film substrates with a mesogenic layer in between with an organic layer comprising immobilized ligands to bind corresponding receptors. Because Gupta is not properly cited as a prior art reference, an anticipation rejection cannot be maintained.

The instant application is a division of application 09/092,452, now abandoned, filed on June 5, 1998. Application 09/092,452 is also the parent of 09/127,382, now U.S. Patent No. 6,284,197 ("the '197 patent"), filed on July 11, 1998. During the prosecution of the '197 patent, Gupta *et al.*, *Science*, **279**:2077-2080 ("Gupta") was cited by the Examiner as an anticipatory reference. In response, Applicants submitted a declaration according to *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982) ("*Katz* declaration"). The anticipatory rejection was withdrawn in light of this *Katz* declaration.

As Gupta was cited in the prosecution of the '197 patent, so it is also cited as an anticipatory reference in the instant application. Since both of these documents share the same

priority date, Gupta cannot serve as a § 102(a) reference here for the same reasons that it was not properly cited as a § 102(a) reference during the prosecution of the '197 patent (see next paragraph for further factual discussion). Therefore, an updated copy of the *Katz* declaration submitted on June 7, 2000 in the '197 patent case is submitted herein as Exhibit A, and Applicants respectfully request withdrawal of the rejection.

Applicants' disclosure of their own work within the year before the application's priority date cannot be used against him under 35 U.S.C. § 102(a). MPEP § 2132.01. The publication can be overcome by submission of a specific declaration by the Applicants establishing that the article is describing Applicants' own work. *Ibid.* In the instant case, Gupta was published in Science on March 27, 1998 and was authored by Vinay Gupta, Justin Skaife, Timothy Dubrovsky, and Nicholas Abbott. Since the instant application is a continuation of application 09/092,452, now abandoned, Gupta was published within a year of the instant application's priority date. Since all four of Gupta's authors are inventors of the instant application, Gupta is a disclosure of the Applicants' own work. Therefore, Applicants submit herein the *Katz* declaration described above (Exhibit A). The declaration is signed by four of the Applicants (Gupta, Skaife, Dubrovsky, and Abbott) and establishes that the Gupta article is describing the Applicants' own work. Again, Applicants respectfully request withdrawal of the rejection.

Under 35 U.S.C. § 102(b)

a) Over Spohn

Claims 66-68 and 109-110 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Spohn (East German Pat. No. DD 278869) and attached CAPLUS AN:1991:243888 ("Conductometric Biosensor for Use in Organic Solvent.") ("Spohn"). Spohn is cited for teaching a biosensor comprising a perfluorinated ethylene-propylene membrane, a polytetrafluoroethylene (PTFE) double membrane organic layer, a lyotropic mesogenic layer, a lipase as a recognition moiety, and a triglyceride as an analyte. However, the cited reference fails to teach all of the claimed elements of the invention. In particular, Spohn does not teach the

following elements of Applicants' invention: "recognition moieties" (Claims 109-110) and "mesogens [which] undergo a detectable switch in orientation" (Claims 66-68).

i) Recognition Moieties

Spohn does not explicitly teach Applicants' recognition moiety element in claims 109-110. Applicants have amended claims 109-110 to explicitly recite the following recognition moieties of the invention: amines, antibodies, nucleic acids, biotin, drug moieties, chelating agents, crown ethers, or cyclodextrins. Since Spohn's teaching of a lipase is not included in the listing above, Spohn does not teach Applicants' recognition moieties. Accordingly, Spohn does not disclose each and every element of claims 109-110. An anticipation rejection, therefore, cannot be maintained.

ii) Mesogenic Shift

Spohn does not teach Applicants' element, in claims 66-68, that "mesogens undergo a detectable switch in orientation" ("mesogenic shift"). In the Applicants' invention, the interaction between a recognition moiety and an analyte introduces a change in the orientation of the organic layer. This change in the organic layer is then transduced to the mesogenic layer. This mesogenic layer comprises mesogens as well as analytes. The mesogens of the mesogenic layer change their orientation in response to the recognition moiety-analyte interaction, and the subsequent change in the intensity of light transmitted through the mesogenic layer is then detected.

By contrast, in Spohn's invention, the recognition moiety is a lipase which hydrolyzes triglycerides to fatty acids. When a triglyceride analyte is introduced, the lipase converts this analyte into fatty acids. The hydrolysis increases the conductivity of the lyotropic mesophase, which is then detected. Therefore, the detected species in Spohn's invention is the hydrolyzed analyte in the mesogenic layer, not the shift in mesogen orientation in the mesogenic layer of Applicant's invention. Spohn's disclosure also does teach that the mesogens in its mesogenic layer are capable of producing a detectable shift in orientation. Since Spohn does not teach Applicant's mesogenic shift, Spohn does not teach each and every element of claims 66-68. An anticipation rejection, therefore, cannot be maintained.

As Spohn does not discuss Applicants' elements of recognition moieties and mesogenic shifts, Spohn does not disclose each and every element of Applicants' invention. Accordingly, an anticipation rejection cannot be maintained, and Applicants respectfully request withdrawal of the rejection.

b) Over Drawhorn

Claims 66-68 and 109-110 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Drawhorn and Abbott, *J. Phys. Chem.*, **99**:16511-16515 (1995) ("Drawhorn"). Drawhorn is cited for teaching, among other things, SAMs with an alkyl group as a recognition moiety. However, the cited reference fails to teach all of the claimed elements of the invention. In particular, Drawhorn does not teach the following elements of Applicants' invention: "recognition moieties" (Claims 109-110) and "mesogens [which] undergo a detectable switch in orientation" (Claims 66-68).

i) Recognition Moieties

Drawhorn does not explicitly teach Applicants' recognition moiety element in claims 109-110. Applicants have amended claims 109-110 to explicitly recite the following recognition moieties of the invention: amines, antibodies, nucleic acids, biotin, drug moieties, chelating agents, crown ethers, or cyclodextrins. These recognition moieties do not include alkyl moieties. Because Drawhorn does not teach Applicants' recognition moieties, Drawhorn does not disclose each and every element of claims 109-110. Therefore, an anticipation rejection cannot be maintained.

ii) Mesogenic Shift

Drawhorn does not explicitly teach Applicants' element, in claims 66-68, that "mesogens [which] undergo a detectable switch in orientation" ("mesogenic shift"). The Examiner has not cited where Drawhorn teaches a mesogenic shift upon interaction between a first recognition moiety and an analyte. Since the Examiner has not demonstrated that each and every element of claim 66-68 is found in Drawhorn, an anticipation rejection cannot be maintained.

Drawhorn also does not inherently teach a mesogenic shift. To establish inherency, two elements must be satisfied. First, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. MPEP § 2112; *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). Thus far, the Examiner has not provided facts or technical reasonings for why the mesogenic layer in Drawhorn would be capable of a mesogenic shift. Therefore, an inherency rejection cannot be maintained.

Second, the missing descriptive matter must be necessarily present as recognized by a person of ordinary skill in the art. MPEP § 2112 and *In re Robertson*, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999) (emphasis added). Inherency may not be established by probabilities or possibilities; the mere fact that a certain thing may result from a given set of circumstances is not sufficient. *Ibid.* Put another way, if the prior art must be optimized in order to possess the Applicants' invention, then the feature is not inherent. MPEP § 2112; *In re Oelrich*, 666 F.2d 578, 581-582, 212 USPQ 323, 326 (CCPA 1981).

In the present case, Drawhorn does not show that its mesogenic layer is capable of producing a mesogenic shift upon the interaction of a recognition moiety with an analyte. As the following section from the instant application demonstrates, a) whether a mesogenic shift occurs, and b) what type of shift occurs, is dependent upon both the concentration of recognition moiety in the SAM and the concentration of the analyte introduced.

... aqueous solutions of Cu^{2+} [analyte] were prepared from $\text{Cu}(\text{ClO}_4)_2$ with concentrations ranging between 1 mM - 20 mM. The gold films supporting SAMs [comprising carboxylic acid recognition moieties] were then immersed for 5 minutes into these solutions of Cu^{2+} below pH 5.5. After removal from the aqueous solution, the surfaces were vigorously dried under nitrogen and then absolute ethanol in order to remove any nonspecifically attached Cu^{2+}

When the concentration of Cu^{2+} in solution was 0.01 mM or less, the alignment of the LC [liquid crystal or mesogenic layer] was uniform and planar (Figure 14A). When the concentration of Cu^{2+} in solution was 0.1 mM and 1mM, the

alignment of the LC was non-uniform and planar (Figure 14B and 14C). When the concentration of Cu^{2+} in solution was 18 mM, the alignment of the LC was homeotropic (Figure 14D).

Example 4, p. 76. Comments added in bold and brackets.

As shown above, constructing a device that produces a) a mesogenic shift and b) the appropriate type of mesogenic shift requires experimentation with analyte and recognition moiety concentrations. Put another way, optimization is required. Therefore, a mesogenic layer does not inherently possess the ability to register Applicants' mesogenic shift. Because Drawhorn does not discuss analytes, or analyte concentration, or removal of nonspecifically attached analytes, or recognition moiety concentration, Drawhorn does not inherently teach a mesogenic layer capable of producing Applicants' mesogenic shift. Therefore, an inherency rejection cannot be maintained.

As Drawhorn does not discuss Applicants' elements of recognition moieties and mesogenic shifts, Drawhorn does not disclose each and every element of Applicants' invention. Accordingly, an anticipation rejection cannot be maintained, and Applicants respectfully request withdrawal of the rejection.

Under 35 U.S.C. § 102(e)

Claims 66-68, 109-111 and 114-117 are rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Matsuda *et al.*, (U.S. Patent No. 6,106,906) ("Matsuda"). Claims 114-117 have been canceled in order to expedite prosecution. Matsuda is cited for teaching a display apparatus comprising a liquid crystal comprising an alignment film on at least one of two opposing substrates wherein the alignment film comprises an 'organic layer' comprising a 'carboxylic acid' or an 'organometallic' compound with displaceable ligands ionically interacting with an 'inorganic ion' with the later formation of a 'polyamide' which is 'rubbed' prior to the addition of a 'mesogenic layer'. However, the cited reference fails to teach all of the claimed elements of the invention. In particular, Matsuda does not teach the following elements: "amine, antibody, nucleic acid, biotin, drug moiety, chelating agent, crown ether, or cyclodextrin recognition moieties", and "[recognition moiety] detectably switch(es) from a first orientation to

a second orientation, thereby transducing said interaction to said mesogenic layer, said transducing causing said mesogenic layer to register a visually detectable feature, whereby said feature is visually detected."

i) Recognition Moieties

Applicants have amended claims 109-110 to recite the following recognition moieties of the invention: amines, antibodies, nucleic acids, biotin, drug moieties, chelating agents, crown ethers, and cyclodextrins. Because Matsuda does not teach amines, antibodies, nucleic acids, biotin, drug moieties, chelating agents, crown ethers, or cyclodextrins as recognition moieties, Matsuda does not disclose each and every element of claims 109-110. Accordingly, an anticipation rejection cannot be maintained.

ii) Mesogenic Shift

Matsuda also does not teach the element that the "[recognition moiety] detectably switch(es) from a first orientation to a second orientation, thereby transducing said interaction to said mesogenic layer, said transducing causing said mesogenic layer to register a visually detectable feature, whereby said feature is visually detected." In the Applicants' invention, the recognition moiety has two states. In the first state, the recognition moiety is not bound to the analyte. In the second state, the recognition moiety is bound to the analyte. For both states, the mesogenic layer is present and registers the change of the recognition moiety from the first state to the second state.

By contrast, in Matsuda, the mesogenic layer registers only one recognition moiety-affected state. This can be explained by examining how Matsuda's invention is formed. Example 34 describes the 'thin film' formation step. From column 34, line 54 to column 35, line 42, the thin film is first prepared by binding the polyamic acid polymer to a metal, spin-coating the film on a silicon wafer, and heating the film to 300 °C. Thus, in the 'thin film formation', the recognition moiety (polyamic acid) changes from its first state (unbound) to its second state (bound) when the analyte (metal) is added. Only after the film is heated and the analyte is bound, is the ferroelectric liquid crystal added (Column 35, line 43). Therefore, the liquid crystal is only transducing the second state (bound) of the recognition moiety. It is impossible for the

liquid crystal to transduce the change from the first to second state in Matsuda because the liquid crystal is not present to record the first state. The visually detected element in this invention is not the change in states of the recognition moiety, but the change in voltage of the film layers. Since it is impossible for Matsuda to transduce a change in its mesogenic layer due to the binding of the analyte to a recognition moiety, this element is missing. Therefore, Matsuda does not disclose each and every element of claims 66-68. Accordingly, an anticipation rejection cannot be maintained.

Since the 'recognition moieties' and 'mesogenic shift' elements of Applicants' invention are not recited by Matsuda, Matsuda does not teach each and every element of the invention. Therefore, an anticipation rejection cannot be maintained and Applicants respectfully request withdrawal of the rejection.

Under 35 U.S.C. § 103(a)

In order to establish a *prima facie* case of obviousness, the rejection must demonstrate that (1) the cited references teach all the claimed elements; (2) there is a suggestion or motivation in the prior art to modify or combine the reference teachings; and (3) there is a reasonable expectation of success. MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). As explained below, the cited references fail to disclose all the elements of the claimed invention and fail to provide a basis for one of skill to either combine the references or reasonably expect that the references' devices could contain Applicants' recognition moieties. Therefore, Applicants respectfully traverse the following rejections.

a) Over Drawhorn in view of Evans

Claims 66-68, 109-110 and 114-115 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Drawhorn, in view of Evans *et al.*, *Faraday Discuss.*, 104:37-48 (1996) ("Evans"). Claims 114 and 115 have already been cancelled in order to expedite prosecution.

(1) The cited references fail to teach all of the claimed elements

The references cited by the Examiner fail to teach all of the claimed elements of Applicants' invention. In particular, neither of the references teach the following elements: 'recognition moieties' and 'mesogenic shifts'.

i) Recognition Moieties

Neither reference teaches a device containing an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a cyclodextrin as a recognition moiety. As discussed above, Drawhorn is cited for disclosing a methyl group as a recognition moiety. Evans is cited for disclosing a carboxylic acid group as a recognition moiety. Neither reference discloses end groups on a self-assembled monolayer aside from methyls and carboxylic acids. Since neither reference discloses an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a cyclodextrin as a recognition moiety, each and every element of claims 109-110 is not disclosed. Accordingly, a *prima facie* case of obviousness cannot be maintained.

ii) Mesogenic Shift

Neither reference explicitly teaches Applicants' element, in claims 66-68, that "mesogens [which] undergo a detectable switch in orientation" ("mesogenic shift"). The Examiner has not cited where Drawhorn or Evans teach a mesogenic shift upon interaction between a first recognition moiety and an analyte. Since the Examiner has not demonstrated that each and every element of claims 66-68 is found in Drawhorn and Evans, an anticipation rejection cannot be maintained.

The references also do not inherently teach a mesogenic shift. As mentioned above, the Examiner must satisfy two elements to establish inherency. The first element is to provide facts/technical reasonings to demonstrate that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Thus far, the Examiner has not provided facts or technical reasonings for why the mesogenic layer in Drawhorn or Evans would be capable of a mesogenic shift. Therefore, an inherency rejection cannot be maintained.

Second, the missing descriptive matter must be necessarily present as recognized by a person of ordinary skill in the art. As mentioned above, as presented in Example 4 of the specification, Applicants' invention requires optimization of the analyte and recognition moiety concentrations, not only to determine the occurrence of a mesogenic shift, but the proper type of mesogenic shift as well. As mentioned above, Drawhorn alone does not provide this teaching. While the Examiner states that the combination of Drawhorn and Evans teach optimization of the liquid crystal device, this optimized variable, SAM chain length, is not the same as Applicants' optimized variables, which are analyte and recognition moiety concentrations. Therefore, the combination of Drawhorn and Evans do not inherently teach a mesogenic layer capable of producing a mesogenic shift. Therefore, an inherency rejection cannot be maintained.

(2) There is no suggestion or motivation to modify or combine the reference teachings

Drawhorn and Evans also fail to suggest the desirability of the claimed device. For example, nowhere in Drawhorn and Evans is there a suggestion that modifying the methyl or carboxylic acid moiety on a self-assembled monolayer will provide an amine-, an antibody-, a nucleic acid-, biotin-, a drug moiety-, a chelating agent-, a crown ether-, or a cyclodextrin-functionalized self-assembled monolayer. In fact, both Drawhorn and Evans are devoid of any reference to Applicants' recognition moieties. Since the references do not mention this element of Applicants' invention, there is no motivation to modify or combine the devices of Drawhorn and Evans in order to produce Applicants' invention.

In addition, Drawhorn and Evans do not suggest the desirability of using their devices to test for analytes. Nowhere in Drawhorn and Evans is there a suggestion that a mesogenic shift could be induced by providing a combination of optimized analyte and recognition moiety concentrations. In fact, both Drawhorn and Evans are devoid of any reference to mesogenic shifts that are induced in this manner. Since neither reference mentions this element of Applicants' invention, there is no motivation to modify or combine the devices of Drawhorn and Evans in order to produce Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

(3) The cited references do not provide a reasonable expectation of success

The references cited by the Examiner fail to provide a reasonable expectation of success in performing the Applicants' invention. As mentioned earlier, Drawhorn and Evans do not disclose a) Applicants' recognition moieties on self-assembled monolayers or b) mesogenic shifts based on analyte-recognition moiety interactions. Since the device of the claimed invention requires these two elements in order to operate, and neither Drawhorn nor Evans contain any reference to these recognition moieties, Drawhorn and Evans do not create a reasonable expectation that their devices can be successfully used for the purpose of Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

Because the cited references fail to teach all the claimed elements, do not contain a suggestion or motivation to modify or combine the reference teachings, and do not provide a reasonable expectation of success, a *prima facie* case of obviousness cannot be set forth. Thus, Applicants respectfully request withdrawal of the rejection.

b) Over Drawhorn in view of Evans and further in view of Cognard

Claims 66-68, 109-111 and 114-115 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Drawhorn, in view of Evans, and further in view of Cognard, *Mol. Cryst. Liq. Cryst.*, 1:1-74 (1982) ("Cognard"). Claims 114 and 115 have already been canceled in order to expedite prosecution. Drawhorn and Evans are cited above. Cognard is cited for teaching the rubbing of polymer substrates, in conjunction with the use of organic surfactants, in order to optimize liquid crystal alignment. For the reasons mentioned below, a *prima facie* obviousness rejection cannot be maintained over the three cited references.

(1) The cited references fail to teach all of the claimed elements

The references cited by the Examiner fail to teach all of the claimed elements of Applicants' invention. In particular, none of the references teach the following elements: 'recognition moieties' and 'mesogenic shifts'.

i) Recognition moieties

None of the references teach Applicants' element, in claims 109-110, of a device containing the recited recognition moieties. In particular, none of the cited references teach an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a cyclodextrin as a recognition moiety. Drawhorn and Evans, as discussed above, do not teach the recognition moieties of the Applicants' invention. While Cognard teaches organic polymer substrates in Table II, page 9-13, there is no disclosure of an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a cyclodextrin as a recognition moiety in the reference. Accordingly, Cognard does not teach the recognition moiety elements of Applicants' invention. Since none of the three references disclose an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a cyclodextrin as a recognition moiety, each and every element of claims 109-110 is not disclosed. Accordingly, the *prima facie* obviousness rejection cannot be maintained.

ii) Mesogenic Shift

None of the cited references explicitly teach Applicants' element, in claims 66-68, that "mesogens [which] undergo a detectable switch in orientation" ("mesogenic shift"). The Examiner has not cited where Drawhorn or Evans or Cognard teach a mesogenic shift upon interaction between a first recognition moiety and an analyte. Since the Examiner has not demonstrated that each and every element of claim 66-68 is found in Drawhorn and Evans, an anticipation rejection cannot be maintained.

The references also do not inherently teach a mesogenic shift. As mentioned above, the Examiner must satisfy two elements to establish inherency. The first element is to provide facts/technical reasonings to demonstrate that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Thus far, the Examiner has not provided facts or technical reasonings for why the mesogenic layer in Drawhorn or Evans or Cognard would be capable of a mesogenic shift. Therefore, an inherency rejection cannot be maintained.

Second, the missing descriptive matter must be necessarily present as recognized by a person of ordinary skill in the art. As mentioned above, as presented in Example 4 of the specification, Applicants' invention requires optimization of the analyte and recognition moiety concentrations, not only to determine the occurrence of a mesogenic shift, but the proper type of mesogenic shift as well. As mentioned above, Drawhorn and Evans do not provide this teaching. Likewise, Cognard discusses the alteration of a mesogenic layer's alignment through rubbing, and not through the binding of an analyte to a recognition moiety. Therefore, an inherency rejection cannot be maintained.

(2) There is no suggestion or motivation to modify or combine the reference teachings

Drawhorn, Evans, and Cognard also fail to suggest the desirability of Applicants' device. As mentioned above, Drawhorn and Evans do not disclose Applicants' recognition moieties. Likewise, Cognard contains no reference to Applicants' recognition moieties. Therefore, the three cited references provide no suggestion that modifying or combining their respective organic layers will provide an amine-, an antibody-, a nucleic acid-, biotin-, a drug moiety-, a chelating agent-, a crown ether-, or a cyclodextrin- functionalized self-assembled monolayer.

In addition, Drawhorn, Evans and Cognard do not suggest the desirability of using their devices to test for analytes. Nowhere in Drawhorn, Evans and Cognard is there a suggestion that a mesogenic shift could be induced by providing a combination of optimized analyte and recognition moiety concentrations. In fact, all three cited references are devoid of any reference to mesogenic shifts that are induced in this manner. Since neither reference mentions this element of Applicants' invention, there is no motivation to modify or combine the devices of Drawhorn, Evans and Cognard in order to produce Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

(3) The cited references do not provide a reasonable expectation of success

The references cited by the Examiner fail to provide a reasonable expectation of success in performing the Applicants' invention. As mentioned earlier, Drawhorn, Evans and

Cognard do not disclose a) Applicants' recognition moieties on self-assembled monolayers or b) mesogenic shifts based on analyte-recognition moiety interaction. Since the device of the claimed invention requires these two elements in order to operate, and since none of the three cited references contain any reference to these recognition moieties, Drawhorn, Evans and Cognard do not create a reasonable expectation that their devices can be successfully used for the purpose of Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

Because the cited references fail to teach all the claimed elements, do not contain a suggestion or motivation to modify or combine the reference teachings, and do not provide a reasonable expectation of success, a *prima facie* case of obviousness cannot be set forth. Thus, Applicants respectfully request withdrawal of the rejection.

c) Over Drawhorn in view of Evans and further in view of Frey

Claims 66-68, 109-110 and 114-117 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Drawhorn, in view of Evans, and further in view of Frey *et al.*, *Anal. Chem.*, **68**:3187-3193 (1996) ("Frey"). Claims 114-117 have already been canceled in order to expedite prosecution. Drawhorn and Evans are described above. Frey is cited for teaching the use of 11-mercaptoundecanoic acid (MUA) for forming monolayers on gold surfaces. For the reasons mentioned below, a *prima facie* obviousness rejection cannot be maintained over the three cited references.

(1) The cited references fail to teach all of the claimed elements

The references cited by the Examiner fail to teach all of the claimed elements of Applicants' invention. In particular, none of the references teach the following elements: 'recognition moieties' and 'mesogenic shifts'.

i) Recognition moieties

None of the references teach Applicants' element, in claims 109-110, of a device containing the recited recognition moieties. In particular, none of the cited references teach an amine, an antibody, a nucleic acid, biotin, a drug moiety, a chelating agent, a crown ether, or a

cyclodextrin as a recognition moiety. Drawhorn and Evans, as discussed above, do not teach the recognition moieties of the Applicants' invention. While Frey discloses poly-lysines covalently attached to self-assembled monolayers in its abstract, Frey is devoid of any reference to amines, antibodies, nucleic acids, biotin, drug moieties, chelating agents, crown ethers, or cyclodextrins as recognition moieties. Therefore, like Drawhorn and Evans, Frey does not disclose this element of Applicants' invention. As the cited references do not disclose all of the elements of Applicants' invention, a *prima facie* case of obviousness cannot be set forth.

ii) Mesogenic Shift

None of the cited references explicitly teach Applicants' element, in claims 66-68, that "mesogens [which] undergo a detectable switch in orientation" ("mesogenic shift"). The Examiner has not cited where Drawhorn or Evans or Frey teach a mesogenic shift upon interaction between a first recognition moiety and an analyte. Since the Examiner has not demonstrated that each and every element of claim 66-68 is found in Drawhorn, Evans and Frey, an anticipation rejection cannot be maintained.

The references also do not inherently teach a mesogenic shift. As mentioned above, the Examiner must satisfy two elements to establish inherency. The first element is to provide facts/technical reasonings to demonstrate that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Thus far, the Examiner has not provided facts or technical reasonings for why the mesogenic layer teachings in Drawhorn, Evans, and Frey would be capable of a mesogenic shift. Therefore, an inherency rejection cannot be maintained.

Second, the missing descriptive matter must be necessarily present as recognized by a person of ordinary skill in the art. As mentioned above, as presented in Example 4 of the specification, Applicants' invention requires optimization of the analyte and recognition moiety concentrations, not only to determine the occurrence of a mesogenic shift, but the proper type of mesogenic shift as well. As mentioned above, Drawhorn and Evans do not provide this teaching. Likewise, Frey does not even teach a mesogenic layer, let alone a mesogenic layer capable of

shifting through the binding of an analyte to a recognition moiety. Therefore, an inherency rejection cannot be maintained.

(2) There is no suggestion or motivation to modify or combine the reference teachings

Drawhorn, Evans, and Frey also fail to suggest the desirability of Applicants' device. As mentioned above, Drawhorn and Evans do not disclose Applicants' recognition moieties. Likewise, Frey contains no reference to Applicants' recognition moieties. Therefore, the three cited references provide no suggestion that modifying the methyl, carboxylic acid, or poly-lysine moiety on a self-assembled monolayer will provide an amine-, an antibody-, a nucleic acid-, biotin-, a drug moiety-, a chelating agent-, a crown ether-, or a cyclodextrin-functionalized self-assembled monolayer. Accordingly, the *prima facie* obviousness rejection cannot be maintained.

In addition, Drawhorn, Evans and Frey do not suggest the desirability of using their devices to test for analytes. Nowhere in Drawhorn, Evans and Frey is there a suggestion that a mesogenic shift could be induced by providing a combination of optimized analyte and recognition moiety concentrations. In fact, all three cited references are devoid of any reference to mesogenic shifts that are induced in this manner. Since neither reference mentions this element of Applicants' invention, there is no motivation to modify or combine the devices of Drawhorn, Evans and Frey in order to produce Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

(3) The cited references do not provide a reasonable expectation of success

The references cited by the Examiner fail to provide a reasonable expectation of success in performing the Applicants' invention. As mentioned earlier, Drawhorn, Evans and Frey do not disclose a) Applicants' recognition moieties on self-assembled monolayers or b) mesogenic shifts based on analyte-recognition moiety interaction. Since the device of the claimed invention requires these two elements in order to operate, and since none of the three cited references contain any reference to these recognition moieties, Drawhorn, Evans and Frey

do not create a reasonable expectation that their devices can be successfully used for the purpose of Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

Because the cited references fail to teach all the claimed elements, do not contain a suggestion or motivation to modify or combine the reference teachings, and do not provide a reasonable expectation of success, a *prima facie* case of obviousness cannot be set forth. Thus, Applicants respectfully request withdrawal of the rejection.

d) Over Gupta in view of Cognard

Claims 66-68 and 109-115 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Gupta in view of Cognard. Both Gupta and Cognard are described above.

As mentioned above, since Gupta is a disclosure of Applicants' own work published within a year before the application filing date, Gupta is not citable as a prior art reference under 35 U.S.C. § 102(a). MPEP § 2132.01. A reference that can not be cited for § 102 purposes also can not be cited as a prior art reference for § 103(a) purposes. MPEP § 2141.01 (I). Therefore, Gupta cannot be part of a *prima facie* obviousness rejection. Since the remaining reference, Cognard, is not cited by the Examiner as teaching all of the elements of Applicants' invention, the *prima facie* obviousness rejection cannot be maintained. Applicants respectfully request withdrawal of the rejection.

e) Over Gupta in view of Frey

Claims 66-68, 109-110 and 114-117 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Gupta in view of Frey. Both Gupta and Frey are described above.

As mentioned above, since Gupta is a disclosure of Applicants' own work published within a year before the application filing date, Gupta is not citable as a prior art reference under 35 U.S.C. § 102(a). MPEP § 2132.01. A reference that can not be cited for § 102 purposes also can not be cited as a prior art reference for § 103(a) purposes. MPEP § 2141.01 (I). Therefore, Gupta cannot be part of a *prima facie* obviousness rejection. Since the remaining reference, Frey, is not cited by the Examiner as teaching all of the elements of

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Applicants' invention, the *prima facie* obviousness rejection cannot be maintained. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Todd Esker
Reg. No. 46,690

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
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